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PHASE 3 SUMMARY OF MRID 00094006:

PRIMARY EYE IRRITATION IN THE RABBIT

STUDY # 2339-81

PRIME+ (FLUMETRALIN)

GUIDELINE REFERENCE:

81-4 PRIMARY EYE IRRITATION IN THE RABBIT

SUMMARY PREPARED BY:

JACQUELINE GILLIS, Ph.D.

MERRILL TISDEL

14 SEPTEMBER 1990

ORIGINAL STUDY PREPARED BY:

STILLMEADOW, INC.

HOUSTON, TEXAS

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STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).

Company: CIBA-GEIGY Corporation (Typed Name)

Company Agent: Thomas Parshley (Typed Name)

Title: Senior Reg. Specialist

Signature: _____ Date: _____

These data are the property of the Agricultural Division of CIBA-GEIGY Corporation, and as such, are considered to be confidential for all purposes other than compliance with FIFRA §10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality which may exist under any other statute or in any other country.

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2339-81

STILLMEADOW, Inc. GLP Compliance Statement

This study was designed and performed in STILLMEADOW, Inc.'s AAALAC accredited laboratory in conformance with Good Laboratory Practice Standards for Nonclinical Laboratory Studies as specified by Department of Health, Education, and Welfare Food and Drug Administration (FR 59986, Dec. 22, 1978).

Robert J. Sabol

Robert J. Sabol
STILLMEADOW, Inc.

This study does not meet the requirements for 40 CFR Part 160 since it was conducted prior to the issuance of the EPA Good Laboratory Practice Standards. It was conducted according to the FDA Good Laboratory Practice Standards as indicated above.

Submitter/Sponsor of Study:

Merrill Tisdel

Merrill Tisdel
Agricultural Division
CIBA-GEIGY Corporation
Greensboro, North Carolina

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Certification of Availability of Raw Data

I hereby certify that the submitter possesses or has access to the raw data used in or generated by the study summarized in this document.

Submitter's Representative: -

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

Certification of Accuracy of Summary and Adequacy of the Study

I certify, in compliance with FIFRA section 4(e)(1)(A), that this summary accurately represents the data presented in the report(s) of this study cited by MRID, and that this study fully satisfies all pertinent requirements of the OPP Guideline it addresses.

Submitter's Representative:

Signature/Date: Merrill Tisdel 10.15.90

Typed Name: Merrill Tisdel

Title: Toxicologist

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Subdivision F
Guideline Ref. No. 81-4
December 24, 1989

81-4 Primary Eye Irritation in the Rabbit

ACCEPTANCE CRITERIA

Does your study meet the following acceptance criteria?

1. N Technical form of the active ingredient tested. (for reregistration only)
2. N Study not required if material is corrosive, causes severe dermal irritation or has a pH of $\leq$ 2 or $\geq$ 11.5.
3.* Y 6 adult rabbits
4. Y Dosing, instillation into the conjunctival sac of one eye per animal.
5.* Y Dose, 0.1 ml if a liquid; 0.1 ml or not more than 100 mg if a solid, paste or particulate substance.
6. NA Solid or granular test material ground to a fine dust.
7. Y/N Eyes not washed for at least 24 hours.
8. Y/N Eyes examined and graded for irritation before dosing and at 1, 24, 48 and 72 hr, then daily until eyes are normal or 21 days (whichever is shorter).
9.* N Individual observations for the entire day of dosing.
10.* N Individual daily observations.

Criteria marked with a * are supplemental and may not be required for every study.

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IDENTIFICATION OF TEST MATERIAL

Chemical Name

CAS Name: N-(2-Chloro-6-fluorobenzyl)-N-ethyl-α,α,α,-trifluoro-2,6-dinitro-p-toluidine

or

2-Chloro-N-[2,6-dinitro-4-(trifluoromethyl)phenyl]-N-ethyl-6-fluorobenzenemethanamine

Common Name: Flumetralin

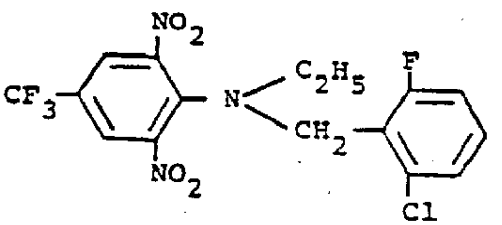
Trade Name: Prime +®

CIBA-GEIGY Code Number: CGA-41065

CAS Registry Number: 62924-70-3

EPA Shaughnessy Number: Unknown

Chemical Structure:



Percent Active Ingredient

Prime +®: 15.0% (Inert, 85.0%)

Identity and Composition of Impurities

Not required for formulated product

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Prime+: 81-4: Primary Eye Irritation in the Rabbit

1. The test article was Prime+ (CGA-41065 15E), a clear orange liquid, FL-810737.

2. The test article is not corrosive, does not cause severe dermal irritation, and does not have a pH less than 2.0 or greater than 11.5.

3. There were six adult New Zealand white rabbits (three males and three females) in the primary "nonwash" group and three male rabbits in the secondary "wash" group.

4. The test material was placed into the conjunctival sac of one eye of each animal by gently pulling the lower lid away from the eyeball to form a cup into which the test material was deposited. The lids were then held together for one second.

5. The dose administered was 0.1 ml of the test material.

6. The test material was a liquid and administered as received.

7. The eyes of the six animals in the nonwash group were not washed. The eyes of the three animals in the wash group were washed with deionized water for one minute beginning 30 seconds after treatment.

8. Both eyes of each animal were examined at least 24 hours prior to treatment with a 0.2% fluorescein sodium ophthalmic solution and again just prior to treatment, but without the fluorescein sodium ophthalmic solution. The treated eyes of all animals were examined and evaluated for irritation at 1, 24, 48, and 72 hours and 4, 7, 10, 13, 16, 19, and 21 days after treatment. Eyes of all nonwash animals had not cleared by Day 21, with corneal involvement persisting until that time. Eyes of two of three wash animals were clear at 16 days, but corneal involvement was apparent in the third animal at 21 days. According to the eye irritation classification scheme, the nonwash treatment was extremely irritating and the wash treatment was severely irritating.

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9. Animals were not observed for pharmacological and/or toxicological effects on the day of dosing.

10. Eye irritation evaluation in the nonwash animals beginning 24 hours after dosing found conjunctival redness, chemosis, and discharge persisted in some animals until Day 21. Corneal opacity and iris involvement persisted in some animals until Day 21.

Average Irritation Scores
Time After Treatment

	Hours				Days						
	1	24	48	72	4	7	10	13	16	19	21
Nonwash	17.7	35.3	44.5	42.3	61.5	51.0	35.7	31.0	27.0	21.2	22.2
Wash	21.0	39.0	34.0	34.0	40.0	21.0	19.7	14.3	7.7	4.0	3.3

Animals were not specifically observed for other pharmacological and/or toxicological effects for the 21 days following the day of dosing.

11. There were no significant deviations from the Acceptance Criteria in this study. Three deviations from the Acceptance Criteria are noted. Under Item 8, the eyes were not graded for irritation each day after Day 4. This deviation is considered to be insignificant because the eyes were examined on Days 7, 10, 13, 16, 19, and 21 and the irritation category would not be affected by changes occurring on intervening days. Under Items 9 and 10, individual observations for toxicity other than eye irritation were not recorded. These criteria are marked as supplemental. In addition, such observations would not substantially enhance the evaluation of potential eye irritation or potential systemic toxicity without the measurement of additional parameters. It is also noted that the test article was the formulated product rather than the technical material. The report of a primary eye irritation study with the technical material (MRID 00094000) is also summarized in this Phase 3 submission.

GILLIS:R512SW0921JG/MT

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